Lis1 regulates asymmetric division in hematopoietic stem cells and in leukemia.

Journal: Nat Genet

Publication Year: 2014

Authors: Bryan Zimdahl, Takahiro Ito, Allen Blevins, Jeevisha Bajaj, Takaaki Konuma, Joi Weeks, Claire S Koechlein, Hyog Young Kwon, Omead Arami, David Rizzieri, H Elizabeth Broome, Charles Chuah, Vivian G Oehler, Roman Sasik, Gary Hardiman, Tannishtha Reya

PubMed link: 24487275

Funding Grants: Interdisciplinary Stem Cell Training Program at UCSD II

Public Summary:
Cell fate can be controlled through asymmetric division and segregation of protein determinants, but the regulation of this process in the hematopoietic system is poorly understood. Here we show that the dynein-binding protein Lis1 is critically required for hematopoietic stem cell function and leukemogenesis. Conditional deletion of Lis1 (also known as Pafah1b1) in the hematopoietic system led to a severe bloodless phenotype, depletion of the stem cell pool and embryonic lethality. Further, real-time imaging revealed that loss of Lis1 caused defects in spindle positioning and inheritance of cell fate determinants, triggering accelerated differentiation. Finally, deletion of Lis1 blocked the propagation of myeloid leukemia and led to a marked improvement in survival, suggesting that Lis1 is also required for oncogenic growth. These data identify a key role for Lis1 in hematopoietic stem cells and mark its directed control of asymmetric division as a critical regulator of normal and malignant hematopoietic development.

Scientific Abstract:
Cell fate can be controlled through asymmetric division and segregation of protein determinants, but the regulation of this process in the hematopoietic system is poorly understood. Here we show that the dynein-binding protein Lis1 is critically required for hematopoietic stem cell function and leukemogenesis. Conditional deletion of Lis1 (also known as Pafah1b1) in the hematopoietic system led to a severe bloodless phenotype, depletion of the stem cell pool and embryonic lethality. Further, real-time imaging revealed that loss of Lis1 caused defects in spindle positioning and inheritance of cell fate determinants, triggering accelerated differentiation. Finally, deletion of Lis1 blocked the propagation of myeloid leukemia and led to a marked improvement in survival, suggesting that Lis1 is also required for oncogenic growth. These data identify a key role for Lis1 in hematopoietic stem cells and mark its directed control of asymmetric division as a critical regulator of normal and malignant hematopoietic development.

Source URL: https://www.cirm.ca.gov/about-cirm/publications/lis1-regulates-asymmetric-division-hematopoietic-stem-cells-and-leukemia